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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/728,355 | 12/05/2003 | Stephen William Watson Michnick | Oddy 004CIP1 | 2697 |

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| ART UNIT | PAPER NUMBER |
|---|---|
| 1639 | |

DATE MAILED: 07/12/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/728,355 | WATSON MICHNICK ET AL. | |
| | Examiner | Art Unit | |
| | Sue Liu | 1639 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *08 May 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-33 and 37* is/are pending in the application.

4a) Of the above claim(s) *6,7,9,10,15,16,18,19 and 25-28* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,8,11-14,17,20-24,29-33 and 37* is/are rejected.

7)☒ Claim(s) *29-33 and 37* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *See Continuation Sheet*.

Continuation of Attachment(s) 6). Other: Notice to Comply (Sequence Rule).

## DETAILED ACTION

**Claim Status**

Claims 34-36 have been cancelled;

Claims 1-33 and 37 are currently pending;

Claims 6, 7, 9, 10, 15, 16, 18, 19, and 25-28 have been withdrawn;

Claims 1-5, 8, 11-14, 17, 20-24, 29-33 and 37 are being examined in this application.

### *Election/Restrictions*

1. Applicant's election with traverse of Group I (claims 1-5, 8, 11-14, 17, 20-24, 29-33 and 37) in the reply filed on 5/8/06 is acknowledged. The traversal is on the ground(s) that there is no serious burden to search all the different groups of invention, and the restriction requirement has failed to that the different inventions are both independent and distinct. This is not found persuasive because of the following reasons:

The previous Restriction Requirement has demonstrated that the different groups of inventions are either distinct or independent (see pages 3-4 of the Restriction Requirement; mailed on 4/7/06). Applicants are respectively invited to see Chapter 800 in MPEP, especially "803 [R-3] Restriction — When Proper", which states that:

> "There are two criteria for a proper requirement for restriction between patentably distinct inventions:
> (A) The inventions must be independent (see MPEP § 802.01, § *>806.06<, § 808.01) **or** distinct as claimed (see MPEP § 806.05 - § *>806.05(j)<); and
> (B) There *>would< be a serious burden on the examiner if restriction is >not< required (see MPEP § 803.02, **> § 808<, and § 808.02)"
> (emphasis added)

Thus, to satisfy the first requirement for a proper restriction, a demonstration of either independent or distinct inventions is sufficient for proper restriction. Following the direction set forth in MPEP, the restriction requirement set forth in previous office action is deemed proper.

In addition, there would also be serious burden to search all the different groups of invention. Even though some of the groups are classified in the same class/subclass, this has no effect on the non-patent literature search. Art anticipating or rendering obvious each of the identified groups respectively would not necessarily anticipate or render obvious another group, because they are drawn to different inventions that have different distinguishing features and/or characteristics. The different methods and products will require completely different searches in both the patent and non-patent databases, and there is no expectation that the searches will be coextensive. Therefore, these do create an undue search burden, and restriction for examination purposes as indicated is proper.

The requirement is still deemed proper and is therefore made FINAL.

2. Claims 6, 7, 9, 10, 15, 16, 18, 19, and 25-28 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 5/8/2006.

3. Applicant's election without traverse of the following species.

(A) Green Fluorescent Protein (GFP) as the fluorescent protein reporter.

(B) The specific fragments of GFP are GFP[1] and GFP[2] as further defined in page 42, line 14.

(C) The species of molecules are protein molecules.

(D) The panels of molecules are two panels of protein molecules.

(E) The quantifiable signal is fluorescent activity.

(F) Directly introducing molecules into cells.

(G) Chemical compounds.

(H) The reporter molecule activity is detected by flow cytometry.

in the reply filed on 5/8/2006 is acknowledged.

Accordingly, the nonelected species are withdrawn from each corresponding claim.

**Sequence Rule Compliance**

4. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR § 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR §§ 1.821 through 1.825 for the reason(s) below:

The instant application does not provide a complete sequence listing. The instant disclosure recites lists of sequences in the drawings (e.g. Figure 2) and the specification (e.g. pg 33), which are not identified by their corresponding SEQ ID Nos. Applicants are requested to amend the instant specification accordingly. Applicants are also invited to see the attached "Notice to Comply" for additional requirements to fully comply with the Sequence Rule.

### *Priority*

5. This application appears to be a CIP of U.S. Patent Application Nos. 09/603,885 (filed 6/26/2000), which is now a US PATENT, 6,897,017 (5/24/2005). The US PATENT, 6,897,017 is a CIP of US Patent Application Nos. 09/017,412 (filed 2/02/1998), which is now a US PATENT, 6,270,964 (8/7/2001). This application also claims priority to U.S. Provisional Patent Application Nos. 60/141,210, filed 6/26/1999.

### *Specification*

6. Applicant is reminded of the proper language and format for an abstract of the disclosure.

The abstract should be in narrative form and generally limited to a single paragraph on a separate sheet within the range of 50 to 150 words. It is important that the abstract not exceed 150 words in length since the space provided for the abstract on the computer tape used by the printer is limited. The form and legal phraseology often used in patent claims, such as "means" and "said," should be avoided. The abstract should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.

The language should be clear and concise and should not repeat information given in the title. It should avoid using phrases which can be implied, such as, "The disclosure concerns," "The disclosure defined by this invention," "The disclosure describes," etc.

### *Claim Objections*

7. Claims 29-33 and 37 are objected to because the said claims depend on non-elected claims. Appropriate correction is required.

### *Claim Rejections - 35 USC § 112*

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it

pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

*Written Description Rejection*

9. Claims 1-5, 8, 11-14, 17, 20-24, 29-33 and 37 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The instant claims recite a method for identifying an interacting set of molecules comprising: A) identifying a first panel and a second panel of molecules whose mutual interaction is desired to be tested; B) coupling molecules of said first panel to first fragments of a fluorescent protein reporter molecule; C) coupling molecules of said second panel to second fragments of said fluorescent protein reporter molecule; wherein said first and second fragments have no activity prior to step (D); D) mixing the products of B) and C); E) directly testing for tluorescent activity of said fluorescent protein reporter molecule; and F) identifying the panel members whose interaction resulted in said fluorescent activity and which thus form an interacting set.

*To satisfy the written description requirement, applicants may convey reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention.*

*Applicants may show possession of an invention by disclosure of drawings or structural chemical formulas that are sufficiently detailed to show that applicant was in possession of the claimed invention as a whole. See, e.g., Vas-Cath, 935 F.2d at 1565, 19 USPQ2d at 1118.*

*The written description requirement of 35 U.SC. 112 exists independently of enablement requirement, and the requirement applies whether or not the case involves questions of priority. The requirement applies to all inventions, including chemical inventions, and because the fact that the patent is directed to method entailing use of compound, rather than to compound per se, does not remove patentee's obligation to provide a description of the compound sufficient to distinguish infringing methods from non-infringing methods. See Univ. of Rochester v. G.D. Searle & Co., 358 F.3d 916, 920-23, 69 USPQ 2d 1886, 1890-93 (Fed. Cir. 2004).*

*With regard to the description requirement, applicants' attention is invited to the decision of The Court of Appeals for the Federal Circuit, which held that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it form other materials." University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1405 (1997), quoting Fiers v. Revel, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (bracketed material in original) [The claims at issue in University of California v. Eli Lilly defined the invention by function of the claimed DNA (encoding insulin)].*

*The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species or by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical an/or chemical properties, by functional characteristics coupled with a known or*

*disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. See Eli Lilly, 119 F. 3d at 1568, 43 USPQ2d at 1406.*

Claims 1-5, 8, 11-14, 17, 20-24, 29-33 and 37 are drawn to a genus of molecules that can be fused with the fragments fluorescent reporter molecule. The instant specification recites that the "panel of molecules" can be "peptide or polypeptide, DNA or cDNA, RNA or siRNA, antibody or single-chain antibody, small-molecule, natural product, and other libraries" (bottome of pg 55 of the instant specification). In other words, the panels of molecules can be almost any biological or chemical compounds, as recited in the specification. The instant specification neither does provide representative number of species, nor provides structural and/or functional limitation for the claimed entire genus of various molecules that can be fused with the reporter molecule.

The only examples provided are fusion molecules between the fragments of the reporter molecule and proteins (including both polypeptides and peptides). However, the instant specification has not demonstrated any fusion molecules between the reporter and any other species of molecules such as DNA and small organic molecules. The instant claimed method relies on molecular cloning technology to construct DNA expression vectors that comprise fusion genes between the genes encoding for the fragments of the reporter molecule, and the genes encoding for the proteins to be tested. The final interaction to be measured is through a protein-protein interaction by measuring the reconstituted fluorescent activity. In order to test panels of molecules that are not protein (encoded by DNA) such as small organic molecules or

DNA themselves, fusion molecules between the reporter molecule fragments and the small organic molecules must be generated (i.e. fusion molecules between proteins and other molecules including DNA and small organic molecules). The instant specification does not teach the generation of such fusion molecules that can be expressed in living cells, and then monitoring the reconstituted fluorescent activity. The state of art also does not teach such methods of generating fusion molecules comprising proteins and other molecules such as small organic molecules in living cells.

Therefore, applicants are not in possession of the entire genus of any molecules that can be fused with the reporter molecule fragments. To provide evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof.

10. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. Claims 2, 4, 5, 8, 12-14, 17, 21-24, 29-33, and 37 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 2, 8, 12, 13, 17, 21, and 24 recite the phrase, "wherein said first and second fragments have no activity..." in Step C (or D) of the claims, which is unclear as to what activity the phrase is referring. The instant specification discloses various "activities" for different

reporter molecules. It is not clear if the "activity" referred in the above said phrase is the same as the "fluorescent activity" in step E) of the claim.

Claims 22 and 23 recite the phrase "wherein fragments", which is unclear as to which fragments the claims are referring. Claims 22 and 23 are dependent on Claims 1-3, 11-13, and 20-21, which recite first and second fragments of a fluorescent reporter molecule. However, it is not clear from the claim language that the recited fragments in Claims 22 and 23 are referring to the first and/or second fragments of the fluorescent reporter. The instant claim 22 can be interpreted to mean that the fragments within the plurality of the "first fragments" have decreased avidity for each other, or that the first fragments have decreased avidity for the second fragments. Similarly, the instant claim 23 can be interpreted to mean that the first fragments (or second fragments) by themselves can product a detectable signal.

Claim 22 recites the term "decreased avidity", which is indefinite because the phrase is a relative term. The claims recite the "decreased avidity" is relative to "a reference set of fragments", which is not clearly defined in either the specification or the claims. Without providing a defined standard or reference set of fragments, the claimed "decreased avidity" cannot be compared, and therefore defined.

Claim 23 similarly recites a relative term, "higher" signal, relative to "a reference set of fragments".

Claim 29 recites the term "said molecules", which is unclear to which molecules the term is referring. Claim 29 depends on Claims 1-3, 8-9, 11-13, 15-18, 20, 21, 24 and 25, which recite different molecules including "first molecules", "second molecules", "fluorescent reporter molecules", "chemical or biological compounds" (which reads on molecules).

***Double Patenting***

12. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

13. Claims 1-5, 8, 11-13, 14, 17, 21-24, and 29-33 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 2, 7, 9-22, 32, 33, 36-38, and 40 of U.S. Patent No. 6,270,964 B1. Although the conflicting claims are not identical, they are not patentably distinct from each other because the '964 patent claim the same method as the instant application.

The '964 patent claims a method for detecting biomolecular interactions using appropriate enzyme reporter molecule that has no reporter activity when fragmented (see Claim 1 of the reference), and the reference also claims the enzyme reporter molecule is a fluorescent probe or protein (see Claims 7 and 40 of the reference). The reference also claims fragmentation

of the enzyme reporter (such as a first and second fragments), and fusing the first and second fragments of the reporter molecules to two different molecules separately, and then detect activity of the reporter molecule upon association of the two different molecules (see Claim 9 of the reference). The claimed methods of the reference read on the method of identifying an interacting set of molecules using fluorescent protein reporters with an optical detectable signal, as recited in **clms 1-3, 8, 11-13, 17, 21, 24, 30, and 31**.

The reference also claims the different molecules that are fused with the first and second fragments of the reporter molecule can be libraries of molecules such as cDNA libraries (see Claim 26 of the reference), which reads on panels of molecules, as recited in **clms 1-5, 8, 11-14, 17, 21, and 24**.

The reference also claims the molecular interactions are conducted in living cells (see Claim 28), which reads on the method step of **clms 32 and 33**.

The reference also claims the second and third molecules are proteins (see Claim 10 of the reference), which reads on the molecules of **clm 29**.

Although the reference does not specifically teaches that fragments have decreased avidity for each other relative to a reference set of fragment as recited in **clm 22,** or that the fragments produce a higher detectable signal than a reference set of fragment as recited in **clm 23**, the decrease avidity and the relative higher signal are inherent properties of the fragments taught by the reference. Neither the instant specification nor the claims define the term "a reference set of fragment", which can be any set of fragment, and therefore the fragments taught by the reference would have the inherent property of decreased avidity where comparing to a reference set of fragments with higher avidity.

***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sue Liu whose telephone number is 571-272-5539. The examiner can normally be reached on M-F 9am-3pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached at 571-272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

SL
Art Unit 1639
7/3/2006

MARK SHIBUYA, PH.D.
PATENT EXAMINER

| Notice to Comply | Application No. 10728355 | Applicant(s) WATSON MICHNICK ET AL. | |
|---|---|---|---|
| | Examiner Sue Liu | Art Unit 1639 | |

## NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

Applicant must file the items indicated below within the time period set in the Office action to which the Notice is attached to avoid abandonment under 35 U.S.C. § 133 (extensions of time may be obtained under the provisions of 37 CFR 1.136(a)).

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

☒ 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). If the effective filing date is on or after July 1, 1998, see the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998).

☒ 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).

☒ 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).

☐ 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."

☐ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).

☐ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).

☒ 7. Other: The instant disclosure recites lists of sequences in the drawings (e.g. Figure 2) and the specification (e.g. pg 33), which are not identified by their corresponding SEQ ID Nos.

### Applicant Must Provide:

☒ An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".

☒ An initial or substitute paper copy of the "Sequence Listing", **as well as an amendment specifically directing its entry into the application**.

☒ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (571) 272-2510
For CRF Submission Help, call (571) 272-2501/2583.
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